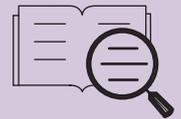


This week's flash update comes from the Emergency Medicine Academic Group in Leicester. EMAG is one of the largest Emergency Care research groups in the UK, encompassing both adult and paediatric emergency care. Research conducted within EMAG ranges from bench research to clinical studies to implementation studies. Our main themes of research are; use of novel devices for illness identification, injury research, clinical data science, geriatric emergency care and paediatric emergency medicine. Check out our website here! We have sorted through thousands of papers, and here are the top 5 papers that deserve your attention.



These have been split into 3 categories that will allow you to focus on the papers that are most vital to your practice.

- Worth a peek: interesting, but not yet ready for prime time
- Head Turner: new concepts
- Game Changer: this paper should change practice

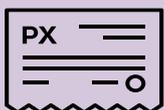
### Multisystem Inflammatory Syndrome in U.S. children and adolescents by Feldstein et al <sup>1</sup>

Topic: Presentation (paediatric)

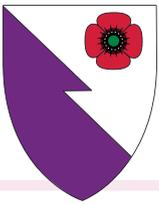
Rating: Head Turner

Scout: Ffion Davies

This surveillance report by the Overcoming COVID-19 Investigators during April and May 2020 is essentially the US version of the UK study published 2 weeks ago (Lancet), with strikingly similar findings. 186 children met criteria for Multisystem Inflammatory Syndrome in Children (MIS-C) – which in the UK is called Paediatric Multisystem Inflammatory Syndrome (PIMS). MIS-C/PIMS shares features with the mysterious Kawasaki disease and toxic shock syndrome, but with additional gastrointestinal (92%) and respiratory (70%) symptoms. Cardiovascular involvement in 80% included coronary artery aneurysms (12%) and, unlike Kawasaki disease, inotropic need was high. Reassuringly for those of us on the front-line MIS-C should be easy to spot as 74% had mucocutaneous symptoms - bilateral conjunctivitis, oral mucosal changes or cervical lymphadenopathy. Headline figures: only 2% died, half with underlying conditions. 27% cases were previously “not healthy”. 62% were male. Startlingly only 19% were in the racial group ‘white, non-Hispanic’. Renal and thromboembolic events were fewer than in adult multi-system Covid-19.



What is still not clear (from either paper) is whether this is an acute viral or a post-viral phase of Covid-19. ED clinical bottom line? These children are Kawasaki-like with additional gastrointestinal and respiratory involvement.



**Risk factors for developing into critical COVID-19 patients in Wuhan, China:  
A multicenter, retrospective, cohort study by Liu et al <sup>2</sup>**

Topic: Prognosis

Rating: Worth a peek

Scout: Mohammed Elwan



Yet another prognostic study, this time with interesting insights on sex as a risk modifier. This is a retrospective cohort study carried out in the COVID-19 designated hospital (two sites) in Wuhan, China. Liu et al. included 2044 Consecutive COVID-19 inpatients discharged (or died) between January and March 2020. Their key finding is that hypertension and coronary artery disease significantly increased the risk of critical illness in males, but not that much in females. Limitations? Many. Retrospective design comes with inherent shortcomings, exclusions were not entirely justified (e.g. excluding 31 patients who died within 24 hours), severity classification requires close reading and an effectively single center study design (although labelled as multi-center, mini-national!) with limited generalisability. What is in it for us? This could be another piece of the conundrum of 'who is not going to do very well with COVID-19', and fits very well with the male preponderance in our ICNARC data. I will be interested to see what future genetic and molecular research will have to say on 'why?' as understanding the increased male risk of poor outcomes may give us insight into mechanisms and treatments.



**COVID-19 and the elderly: insights into pathogenesis and clinical  
decision-making by Perrotta et al <sup>3</sup>**

Topic: Geriatric emergency medicine

Rating: Worth a peek

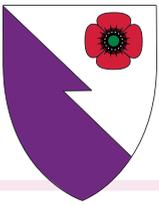
Scout: James van Oppen



We know already that people aged over 80 develop ARDS more frequently and have greater risk of dying from COVID-19, and that age itself may be a greater predictor than frailty. This paper reviewed the pathophysiology and clinical features of coronaviruses affecting older people. As in younger people, COVID-19 symptoms are commonly fever and productive cough, and less commonly include headache and diarrhoea. Older people, however, frequently have atypical presentations of illness: COVID-19 may present as delirium or abdominal pain. Their lab tests frequently show lower lymphocyte proportions and higher CRP, and radiography more commonly demonstrates multi-lobe involvement compared to younger people.

Risk balance of use of drugs needs to be carefully evaluated as adverse effects may be more common in older people. The article also highlights that in our communication with patients and their carers, we should also bear in mind the 'adverse effects' caused by social distancing, such as anxiety, delirium, and accelerated cognitive decline particularly among those people living with dementias.





### **Nebulised heparin as a treatment for COVID-19: scientific rationale and a call for randomised evidence by Van Haren et al <sup>4</sup>**

Topic: Treatment

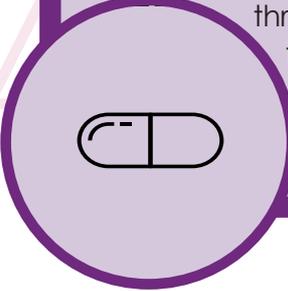
Impact rating: Head Turner

Scout: Mohamed Morsy



The authors in this review highlight the theoretical benefits of using nebulized unfractionated Heparin (UFH) for COVID-19, including antiviral, anticoagulant, anti-inflammatory and mucolytic effects. In particular the high prevalence of microvascular thrombosis might be treated by nebulised heparin. They point out previous studies on acute lung injuries such as smoke inhalation. Additionally, the authors suggest that binding of UFH with SARS-COV-2 Spike S1 protein receptor results in a conformational receptor change. This change may inhibit binding of SARS-Cov-2 to Angiotensin-converting enzyme-2 (ACE-2) and potentially may prevent the process of viral cellular entry.

The authors propose that administration of nebulized UFH in hospitalised patients throughout the course of COVID-19 infection may mitigate the disease progression to COVID-pneumonitis and ARDS. They make an urgent call for the current clinical trials investigating nebulize UFH (which includes ACCORD in the UK), to link together into a global large-scale meta-trial to test for clinical benefits from this inexpensive and well-known drug.



### **Pandemic peak SARS-CoV-2 infection and seroconversion rates in London frontline health-care workers by Houlihan et al <sup>5</sup>**

Topic: Frontline staff prevalence

Rating: Head Turner

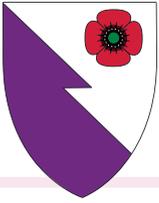
Scout: Tim Coats



In this first report from the SAFER study 200 front line healthcare workers were studied over a two week period at the beginning of the COVID-19 wave in London. 44% had evidence of SARS-CoV-2 infection – more than double the local general population. Of the 36 healthcare workers who seroconverted during the study only half had a positive swab. In the 42 with positive swabs 38% had no symptoms in the proceeding 7 days. The study is ongoing and extending to more frontline staff nationwide.

This was at the beginning of our experience with COVID19, so ED staff may now be better protected both at work and at home. However, these results show that we are in a high-risk group, implying a need for continuing vigilance on PPE use and emphasis on high-touch surface cleaning routines in EDs. The positive swabs in asymptomatic frontline workers suggests that routine testing of ED staff should be part of a response to a 'spike' in local community prevalence.





### In summary

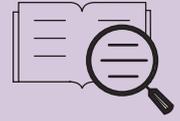
Feldstein et al warned of a 'Kawasaki like' hyperinflammatory syndrome in children <sup>1</sup>

Liu et al described the interaction between sex and comorbidities <sup>2</sup>

Perrotta et al reviewed the differences in characteristics of COVID-19 among older people <sup>3</sup>

Van Haren et al highlighted the need for a global trial of nebulised unfractionated heparin <sup>4</sup>

Houlihan et al showed a high prevalence of SARS-CoV-2 infection in UK frontline healthcare staff <sup>5</sup>



### References

1) Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *New England Journal of Medicine* 2020;383(4):334-46. doi.org/10.1056/NEJMoa2021680

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3) Perrotta F, Corbi G, Mazzeo G, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clinical and Experimental Research* 2020 doi.org/10.1007/s40520-020-01631-y

4) van Haren FMP, Page C, Laffey JG, et al. Nebulised heparin as a treatment for COVID-19: scientific rationale and a call for randomised evidence. *Critical Care* 2020;24(1):454. doi.org/10.1186/s13054-020-03148-2

5) Houlihan CF, Vora N, Byrne T, et al. Pandemic peak SARS-CoV-2 infection and seroconversion rates in London frontline health-care workers. *The Lancet* 2020;396(10246):e6-e7. doi.org/10.1016/S0140-6736(20)31484-7

